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APPLICATION NUMBER:

21-143

PHARMACOLOGY REVIEW

CLINICAL PHARMACOLOGY/BIOPHARMACEUTICS REVIEW

NDA: 21-143

SUBMISSION DATE: June 16, 1999

Clotrimazole Vaginal Cream, 2%

REVIEWER: Funmilayo Ajayi, Ph.D.

Taro Pharmaceuticals Inc.
130 East Drive, Bramalea, Ontario
L6T 1C3 Canada

TYPE OF SUBMISSION: Original NDA

Background: This submission is for a 3-day treatment of vaginal candidiasis. Cross reference is made to Schering Plough's approved Clotrimazole Vaginal Cream, 2% product (NDA 20-574).

Findings: The formulas of Schering Plough's 2% cream formulation (Gyne-Lotrimin 3) and Taro's Clotrimazole Vaginal Cream, 2% are slightly different. However, a bridging clinical study, performed between Taro's 2% cream formulation and Schering Plough's 2% cream formulation, served as one of the basis for the 11/25/98 approval of Schering Plough's product.

Review of the original Schering Plough's NDA 20-574 for Clotrimazole Vaginal Cream, 2% was performed by Dr. Ette in August 1995.

Recommendation: Since the to-be-marketed product was a subject of an approved NDA 20-574, no further clinical pharmacology and biopharmaceutics study is indicated.

IS/ 8/31/99
Funmilayo O. Ajayi, Ph.D.
Div. of Pharmaceutical Evaluation III
Office of Clin. Pharmacol. & Biopharmaceutics

FT signed by Arzu Selen, Ph.D. (Deputy Director, DPE3, OCPB)

cc: NDA 21-143, HFD-590 (Clinical Division)
HFD-880 (Selen, Ajayi)

/S/

8/31/99

KEY WORDS: Clotrimazole vaginal cream USP, 2%, Taro

Reviewer Name: Owen McMaster

Division Name: Division of Special Pathogen and Immunologic Drug Products

HFD#590

Review Completion Date: February 8, 2000

NDA number: 21-143

Related IND: [REDACTED]

Related DMF: [REDACTED]

Submission date: June 17, 1999

Sponsor: Taro Pharmaceuticals Inc., 130 East Drive, Bramalea, Ontario L6T1C3

Manufacturer (drug substance): [REDACTED]

Generic Name: clotrimazole

Trade Name: Trivagizole-3

Chemical Name: 1-(*o*-Chloro- α,α -diphenylbenzyl)imidazole

CAS Registry Number: 23593-75-1

Molecular Formula: C₂₂H₁₇ClN₂

Molecular Weight: 344.84

Related NDA: 20-574

Drug Class: Clotrimazole is a synthetic organic antifungal agent of the imidazole class of drugs.

Indication: 3-day treatment of vaginal candidiasis. (OTC)

Clinical formulation:

Trivagizole-3 cream contains 2-octyldodecanol NF [REDACTED] cetostearyl alcohol [REDACTED] cetyl esters wax NF [REDACTED] polysorbate-60 NF [REDACTED] sorbitan monostearate NF [REDACTED] purified water USP [REDACTED] benzyl alcohol NF [REDACTED] and clotrimazole (2 %).

Background

Schering-Plough HealthCare Products (SPHCP) recently received approval from the FDA to market Gyne-Lotrimin 3[®] 3-Day Vaginal Cream, containing clotrimazole, 2 %. SPHCP has granted Taro Pharmaceuticals Inc. the right to reference all safety and efficacy data (including preclinical Pharmacology and Toxicology data) contained in the NDA for Gyne-Lotrimin 3[®] 3-Day Vaginal Cream. No Pharmacology or Toxicology data was submitted to this NDA for Trivagizole-3, since the Schering product is almost identical to the Taro product (see Table 1).

Table 1: Formula comparison of Taro and Schering clotrimazole creams USP 2 %.

Ingredient	Function	Schering	Taro
		% w/w	% w/w
2-octyldodecanol, NF			
Cetostearyl alcohol			
cetyl esters wax NF			
Polysorbate-60 NF			
Sorbitan monostearate NF			
Purified water USP			
Benzyl alcohol NF			
Clotrimazole	Active ingredient	2.0	2.0

Recommendations

The active ingredient of Trivagizole-3, clotrimazole, is present in a number of approved products, including the recently approved Gyne-Lotrimin 3[®] 3-Day Vaginal Cream (which also contains 2% clotrimazole). The difference between the Schering and the Taro products is not expected to result in any marked changes in the toxicity profile of the clotrimazole formulation. None of the available data regarding use of clotrimazole preparations precludes the approval of Trivagizole-3 for the over the counter use as a 3-day treatment for vaginal yeast infections.

/S/

Owen G. McMaster, Ph.D.
Pharmacology/Toxicology Reviewer, DSPIDP

Concurrences:

HFD-590/Ralbrecht

HFD-590/KHastings:

Disk:

HFD-590/KHastings

cc:

HFD-590 Original IND

HFD-590/PM/CChi

HFD-590 Division File

HFD-590/Micro/LGosey

HFD-340

HFD-590/MO/JWinfield

HFD-590/Bio/FAjayi

HFD-590/Pharm/OMcMaster

HFD-590/Chem/DMatecka

3/20/00

3/15/00